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**REMARKS/ARGUMENTS**

Claims 1-14, and 20-21 are presently examined on the merits. The remaining claims that are presently withdrawn are hereby cancelled without prejudice.

Applicants address below the claim rejections asserted in the Office Action. The cites to the Application as provided hereinbelow refer to the present Application as filed, and they are given for illustrative purposes, but not as interpretive limitations. In addition, such cites are not meant to be the only passages in the Application that are pertinent to the discussed subject matter, but they are intended as examples of the written description provided in the specification. Additional descriptive material can be found in the specification. Furthermore, and given the numerous cites given below, cites that could be used more than once to illustrate written description of more than one type of subject matter have been provided only once to keep the remarks below concise.

Claims 1 and 21 have been amended to clarify their language and also to highlight features of the claimed methods. Support for these amendments can be found in the Application as filed. *See, e.g.,* Application, p. 17, ll. 20-21; p. 10, ll. 20-21, p. 11, ll. 1-7, p. 13, ll. 15-17, p. 14, ll. 16-18, p. 16, ll. 1-2, 10-11, and further description of examples and of the practice of the claimed methods.

The rejections of claims 1-14 under 35 U.S.C. § 112 ¶ 2 are respectfully traversed on at least the grounds provided below. It is respectfully submitted that the Office Action does not establish that such claims are indefinite.

Applicants reassert the grounds and reasoning for traversing these rejections as set forth in the prior response dated April 12, 2002. In addition, for at least the reasons set forth below, Applicants submit that the present claim recitations set out and circumscribe the claimed subject

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matter with a reasonable degree of clarity and particularity, thus satisfying the requirements under 35 U.S.C. § 112.

The claims recite, *inter alia*, “determining the level of resistance of HIV to the HIV RT inhibitor by comparing the RT activity of the wild-type RT enzyme with the RT activity of the mutant RT enzyme”. The claim recitation continues by providing that the “RT activity” is determined “by measuring the amount of the detectable dNTP substrate incorporated into the template”. Further claim recitation concerns the detectable dNTP substrate and the template. Because the claims recite what comparisons are performed and the entities involved in such comparisons, the claims set out with a reasonable degree of clarity and particularity the claimed subject matter.

The Office Action inquires about “which specific activities (i.e., primer extension, fidelity, chain-terminating nucleotide removal, etc.) of the RT are being examined to ascertain the ‘level of resistance’.” If the Office Action intends to inquire on the description by Applicants of the theories, reasons for the invention to work, and/or how the invention was made, Applicants respectfully submit that such inquiry has clearly been disqualifed and has been declared to be not part of the patentability analysis.<sup>1</sup>

Applicants have established that the claimed methods are free from a number of limitations.<sup>2</sup> As noted in the prior Response dated April 12, 2002, one of ordinary skill in the

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<sup>1</sup> It is well established law and also internal PTO patent examination procedure that “[a]n inventor does not need to know how or why the invention works in order to obtain a patent.” (Citing *Newmann v. Quigg*, 877 F.2d 1575, 1581, 11 U.S.P.Q.2d 1340, 1345 (Fed. Cir. 1989)) Guidelines for Examination of Patent Applications Under the 35 U.S.C. § 112 ¶ 1, “Written Description” Requirement, 66(4) Fed. Reg. 1099, 1103 (January 5, 2001). Furthermore, “[t]here is no statutory basis to require disclosure of why an invention works or how it was developed. ‘Patentability shall not be negatived by the manner in which the invention was made.’” (Quoting 35 U.S.C. § 103(a)). 66(4) Fed. Reg. 1099, 1103.

<sup>2</sup> Illustrations of such numerous passages are provided by the following cites: *See, e.g.*, Application, p. 4, ll. 15-20, p. 5, ll. 9-10 (concerning, *inter alia*, forms of expression for degree of susceptibility in the context of the claimed methods); Application, p. 11, ll. 19-20 (concerning, *inter alia*, assays that can be performed in the context of the claimed methods); Application, p. 12, ll. 21-22, p. 13, ll. 1-4, p. 14, ll. 19-20 (concerning, *inter alia*, the natural substrate or sequence of template-primer, type of template, and cell culture or other phenotypic assays in the context of the claimed methods); Application, p. 14, ll. 4-12 (concerning, *inter alia*, applicability of

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art will recognize that the claimed methods are not limited by specific types of controls, and that the scope of the types of controls that may be used with the claimed methods may be determined with reasonable degree of certainty in light of the ordinary skill in the art and the description provided in the present Application. In this regard, Applicants note that the breadth of a claim is not to be equated with indefiniteness. *See, e.g., In re Miller*, 441 F.2d 689 (C.C.P.A. 1971).

Claim 14 has been amended to make it directly dependent from claim 1, and to clarify its language. The reason for its compliance with 35 U.S.C. § 112 ¶ 2 as set forth in the Response dated April 12, 2002, is reasserted. The scope of claim 14 has not been reduced with respect to that of its original recitation.

Regarding the characterization of what in the Office Action is termed as the claim preceding claim 14, and which is understood to mean claim 13, Applicants note that this claim is to be characterized in terms of its recitation. This is to say, the method of claim 1, "wherein the mutant RT enzyme contains mutations at codons 67, 69 and 70." Patentability of this claim has not been questioned under a separate ground pursuant to 35 U.S.C. § 112 ¶ 2, and this claim scope is not to be limited by any extraneous characterization.

Applicants respectfully submit that in, light of the foregoing reasons, the pending claims satisfy the requirements under 35 U.S.C. § 112 ¶ 2 and request the removal of these rejections.

The rejections of claims 1-14 and 20-21 under 35 U.S.C. § 103(a) are respectfully traversed on at least the grounds provided below. It is respectfully submitted that the Office Action does not establish a *prima facie* case of obviousness.

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high throughput analysis in the context of the claimed methods); Application, p. 15, ll. 3-14 (concerning, *inter alia*, embodiments of detectable dNTP and tracers in the context of the claimed methods); Application, p. 15, ll. 15-22 (concerning, *inter alia*, embodiments of HIV RT inhibitors in the context of the claimed methods); Application, p. 16, ll. 10-13 (concerning, *inter alia*, embodiments of reaction initiation and of HIV RT enzymes in the context of the claimed methods).

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Applicants reassert the grounds and reasoning for traversing these rejections as set forth in the prior response dated April 12, 2002. In addition, for at least the reasons set forth below, Applicants respectfully submit that the pending claims are not obvious in light of the art of record.

Claims 1 and 21, and by incorporation its dependent claims, have been amended to include, *inter alia*, the recitation of "performing an enzymatic kinetics assay that permits the measurement of multiple primer chain termination events". This recitation is introduced to make more apparent in the claims nonlimiting distinguishing features.

Even if the cited references where combinable, the Office Action provides no reasons for *w2c46* the motivation to combine them and for the expectation of success. The Office Action appears to identify reference pieces of disclosure according to the blueprint provided by the claimed methods, and collate such pieces together with the contention that it would have been obvious to one having ordinary skill in the art to combine the references in such a way as to generate the claimed methods.

Applicants note first that some of the authority relied on by the Office Action has been distinguished and limited in its applicability by the Federal Circuit. For example, the holding in *In re Bozek*, 416 F.2d 1385, 163 U.S.P.Q. 545 (C.C.P.A. 1969), has been defined by the Federal Circuit as follows: (a) "*Bozek* did not hold that common knowledge and common sense are a substitute for evidence, but only that they may be applied to analysis of the evidence." *In re Lee*, 61 U.S.P.Q.2d 1430, 1435 (Fed. Cir. 2002). (b) "*Bozek* did not hold that objective analysis, proper authority, and reasoned findings can be omitted from Board [of Patent Appeals and Interferences] decisions." *Id.* (c) "Nor does *Bozek*, after thirty-two years of isolation, outweigh the dozens of rulings of the Federal Circuit and the Court of Customs and Patent Appeals that determination of patentability must be based on

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evidence." *Id.* (d) "This court has remarked ... that *Bozek*'s reference to common knowledge 'does not in and of itself make it so' absent evidence of such knowledge."

(Quoting *Smiths Industries Medical Systems, Inc. v. Vital Signs, Inc.*, 183 F.3d 1347, 1356, 51 U.S.P.Q.2d 1415, 1421 (Fed. Cir. 1999)). *In re Lee*, 61 U.S.P.Q.2d 1430, 1435 (Fed. Cir. 2002) (vacating and remanding holding of obviousness by US PTO Board of Patent Appeals and Interferences). The holding of obviousness by the Board was based, *inter alia*, on the erroneous proposition that "[t]he conclusion of obviousness may be made from common knowledge and common sense of a person of ordinary skill in the art without any specific hint or suggestion in a particular reference", and where the "Board did not explain the 'common knowledge and common sense' on which it relied for its conclusion that 'the combined ... [references] would have suggested the claimed invention to those of ordinary skill in the art.'"

*In re Lee*, 61 U.S.P.Q.2d at 1432 (Fed. Cir. 2002).

Current legal authority clearly requires findings of and establishing the specific sources and the specific evidence of the motivation to combine references.

The Office Action contends that some elements of the claimed methods are disclosed in a combination of references and then asserts a broad conclusory statement to the effect that "it would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to utilize ... [some element of one reference] in ... [another element] of some other reference], since this provides a rapid, quantitative, and non-radioactive means for detecting the products of reverse transcription." Office Action, pp. 4, 6-7. This type of rejection fails to establish a *prima facie* case of obviousness for at least two reasons.

First, and although the suggestion to combine may be found in the ordinary knowledge of those skilled in the art, "there still must be evidence that 'a skilled artisan, confronted with the same problems as the inventor and with no knowledge of the claimed

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Serial No. 09/599,877 invention, would select the elements from the cited prior art references for combination in the manner claimed.”” (Quoting *In re Rouffet*, 149 F.3d 1350, 1357 (Fed. Cir. 1998). *Ecolochem, Inc. v. Southern California Edison*, 56 U.S.P.Q.2d 1065, 1075-76 (Fed. Cir. 2000) (reversing the district court’s ruling of claim invalidity for obviousness because of clear error in the district court’s finding that there was motivation to combine the teachings of the prior art references, and establishing that specific sources and specific evidence of the motivation to combine prior art references must be convincingly discussed and identified, and that broad conclusory statements regarding the teaching of multiple references are not evidence).

In contrast with what is predicated in the Office Action, an obviousness rejection that is purportedly based on a combination of references “cannot be predicated on the mere identification … of individual components of claimed limitations. Rather, particular findings must be made as to the reason the skilled artisan, with no knowledge of the claimed invention, would have selected these components for combination in the manner claimed.”

*In re Kotzab*, 217 F.3d 1365,1371 (Fed. Cir. 2000). Findings of and reasons for the combination must still be made of record without relying on the present Application. Furthermore, the question of motivation to combine “[cannot] be resolved on subjective belief and unknown authority.” *In re Lee*, 61 U.S.P.Q.2d at 1434 (Fed. Cir. 2002). The Office Action does not provide such reasons and findings without relying on the disclosure provided in the present Application. Instead of providing such findings and reasons, the Office Action cites characteristics of the claimed methods and advantages of the same methods to allege that a *prima facie* case of obviousness has been established. This matter is addressed in the second reason provided below.

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The reasoning in the Office Action has already been disqualified as part of an analysis under 35 U.S.C. § 103(a): “It is improper, in determining whether a person of ordinary skill would have been led to this combination of references, simply to ‘[use] that which the inventor taught against its teacher.’” (Quoting *W.L. Gore v. Garlock, Inc.*, 721 F.2d 1540, 1553 (Fed. Cir. 1983)). *In re Lee*, 61 U.S.P.Q.2d at 1434 (Fed. Cir. 2002). In addition, using the characteristics and advantages of the claimed methods as a motivation to combine appears in contravention of the principle that “[d]efining the problem in terms of its solution reveals improper hindsight in the selection of the prior art relevant to obviousness.” (Quoting *Monarch Knitting Mach. Corp. v. Sulzer Morat Gmbh*, 139 F.3d 877, 880 (Fed. Cir. 1998)). *Ecolochem, Inc. v. Southern California Edison*, 56 U.S.P.Q.2d 1065, 1073 (Fed. Cir. 2000). Furthermore, a showing of a teaching or motivation to combine references is required because “[c]ombining prior art references without evidence of such a suggestion, teaching, or motivation simply takes the inventor’s disclosure as a blueprint for piecing together the prior art to defeat patentability—the essence of hindsight.” (Quoting *In re Dembicza*k, 175 F.3d 994, 999 (Fed. Cir. 1999)). *Ecolochem, Inc. v. Southern California Edison*, 56 U.S.P.Q.2d 1065, 1073 (Fed. Cir. 2000).

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Lack of motivation to combine references is particularly significant in a field such as that of the claimed methods. Even the cited references themselves evince that the understanding of the processes involved in the development of HIV resistance to an HIV RT inhibitor, and the results obtained with the various techniques reported therein were not clear in light of such references. In addition, the references are actually in disagreement with one another. For example, Meyer, *et al.*, (1999) (one of the cited references) report that their “results do not agree with those of Arion et al. (1998) [another of the cited references]” and further specify that they “do not understand the reason for this difference.” Meyer, *et al.*, p.

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41, left col. (1999). *See also, e.g.*, Application, p. 6, ll. 8-18, p. 12, ll. 9-17. It is particularly unclear in the field of HIV resistance and in light of this status of the art, how motivation to combine and expectation of success can be found without resorting to the blueprint presented by the Application itself. The choice and combination of the elements and features recited in the presently claimed methods cannot be used to assert an obviousness rejection by relying on such choice and combination to select and assemble references.

Applicants respectfully submit that a *prima facie* case of obviousness under 35 U.S.C. § 103(a) for the pending claims has not been established, and request the removal of these rejections.

Attached hereto is a marked-up version of the changes made to the specification and claims by the current amendment. The attached page(s) is/are captioned "Version with markings to show changes made".

Applicants respectfully request that a timely Notice of Allowance be issued in this case.

Respectfully submitted,



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Dated: February 21, 2003